REMARKS

After entry of this Preliminary Amendment, Claims 1-10 and 83-86 are pending and are directed to methods of altering the immunoreactivity of human cells by transfecting genes that encode accessory molecule ligands into cells so that the gene products are functionally expressed. In the previous final action, the Examiner rejected each of the claims on 35 USC §§ 112, 102, and 103 grounds. Also objected to are the Declaration, Title, Drawings, Abstract, Seq. ID numbering, and the specification as relates to spelling errors and lack of trademark indication.

The Declaration has already been changed to comply with 37 CFR 1.67(a) as determined by the Examiner. A copy of the previously submitted Declaration is attached to this action.

Rejections under 35 USC §112

In the previous office action, the Examiner rejected claims 1-7, 67, and 83 for allegedly failing to describe "in such full, clear, concise, and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention." The Examiner focuses on the meaning of the claim term "ligand" and states that it is a relative term that is vague, unclear, and has an insufficient biochemical characterization (e.g., molecular weight, amino acid composition, N-terminal sequence, etc) for purposes of supporting the claims. The Examiner alleges that the term encompasses a "myriad of molecules" that is not enabled and would lead to undue experimentation for one of skill in the art seeking to practice the claims. This rejection is fully met by the amendment of the claims requiring that the accessory molecule ligand is derived from a member of the TNF family.

In light of the above, the Applicants respectfully request that the Examiner not reassert this rejection against the pending claims.

Rejections under 35 USC §§ 102 and 103

The Examiner has previously rejected the pending claims 1-8, 10 and 83 over 35 USC §102(b) as allegedly anticipated by Yellin et al. (J. Immun., 1994). The Examiner states that Yellin teaches that "transfecting cells, including leukemia cells, with CD40 ligand enhances a cell costimulatory activity." However, this is incorrect.

Yellin shows CD40-L specific effects on B cell isotype secretion mediated by supply of CD40-L signals to an entirely different cell type (CD40-L$^+$ Jurkat T cell lymphoma D1.1). Yellin, pg. 2166, col 2, ¶ 2. The Applicant has thoroughly read and fails to note any mention of transfection of the gene encoding the accessory molecule ligand, CD40-L, into the cells that become immunostimulated. The CD40-L transfected cells in Yellin do not become immunostimulated and Yellin did not test for such immunostimulation. Further, the claim amendments clarify that it is the gene encoding the accessory molecule ligand that is transfected into the human cells and which results in the increased stability of the accessory molecule ligand on the surface of these cells. These limits are not present in the Yellin reference.

The Examiner has previously rejected pending claims 1-10, and 83 under 35 USC §102(b) over Alderson et al. (J. Exp. Med., 1993) stating: "Alderson et al. teach that CD40 ligand transfected cells induce monocytes to become tumoricidal" and "transfection with either murine or human CD40 ligand." However, the Applicants' reading of Alderson does not show transfection of an accessory molecule ligand gene into a *human* cell line as required by each of Applicants' claims. Alderson instead teaches transfection of cell line CV-1, which is a monkey, and not a human, cell line. Furthermore, Alderson, at page 671, teaches cellular adhesion of monocyte cells and tumoricidal induction of the same by contact with transfected cells of an entirely different origin. Alderson thus teaches intercellular effects and applications, and not the initial intracellular signaling that Applicants' claims teach. Finally, Alderson fails to teach the increased stability of the accessory molecule ligand as required by the Applicants' amended claims.

Finally, the Examiner had previously rejected claims 1-7 and 83 under 35 USC §102(e) over US Patent 5,861,310 ("the '310 patent") issued to Freeman. The Examiner states that "Freeman et al. teach altering the reactivity of a cell...by introducing a gene encoding an accessory molecule ligand (B7) alone or together, that is to be expressed on the cell surface."

The submitted claim amendments require that the accessory molecule ligand be derived from a member of the TNF family. Because B7 is not a member of the TNF family, this reference is no longer applicable.

In light of above clarification of the claims over the cited art, the Applicants respectfully submit that patentable differences over the art exist that the previously stated rejections are no longer applicable. This applies not only to the rejections founded on §102 grounds, but also to those

rejections founded on §103 grounds as well. The references' combined teachings in no way teach or suggest the claimed invention, and therefore do not amount to legal obviousness. To capitulate, the references teach transfection of cells with genes that encode accessory molecules that are characteristic of *normal expression in those very cell types*. The Applicants' invention is different in that it teaches the useful transfection of (accessory molecule ligand) genes that are not functionally expressed in cells which express the corresponding and complementary accessory molecules. As noted above, the art and the specification communicate a clear distinction between accessory molecules and accessory molecule ligands.

Conclusion

For the forgoing reasons, it is respectfully submitted that the claims as written are clear, enabled, and not anticipated nor rendered obvious by any of the references cited. It is therefore respectfully requested that such grounds of denial for a patent on the subject claims be withdrawn.

Respectfully submitted,

LYON & LYON LLP

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By: _____
Jeffrey W. Guise
Reg. No. 34,613

633 West Fifth Street, Suite 4700
Los Angeles, California 90071-2066
(213) 489-1600